IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

HERON THERAPEUTICS, INC.,	§	
	§	
Plaintiff,	§	
	§	
v.	§	Civil Action No. 22-985-WCB
	§	
FRESENIUS KABI USA, LLC,	§	
	§	
Defendant.	§	
	§	
	§	

CLAIM CONSTRUCTION ORDER

In this Hatch-Waxman Act patent case, plaintiff Heron Therapeutics, Inc., ("Heron") alleges that defendant Fresenius Kabi USA, LLC, ("Fresenius") infringes various claims of six patents: U.S. Patent No. 9,561,229 ("the '229 patent"); U.S. Patent No. 9,808,465 ("the '465 patent"); U.S. Patent No. 9,974,793 ("the '793 patent"); U.S. Patent No. 9,974,794 ("the '794 patent"); U.S. Patent No. 10,500,208 ("the '208 patent"); and U.S. Patent No. 10,953,018 ("the '018 patent"). The asserted claims are directed to stable, injectable formulations of aprepitant, a compound that is used to treat chemotherapy-induced nausea and vomiting ("CINV"). Heron alleges that its branded drug CINVANTI is a commercial embodiment of the asserted claims. Dkt. No. 1 ¶¶ 32–34.

For purposes of resolving the parties' claim construction disputes, claim 1 of the '794 patent and claim 1 of the '465 patent are representative.

Claim 1 of the '794 patent recites as follows:

> 1. A *physically stable* pharmaceutical composition comprising:
> 0.4 wt/wt % to 1.0 wt/wt % aprepitant;
> 13 wt/wt % to 15 wt/wt % egg yolk lecithin;
> 9 wt/wt % to 10 wt/wt % soybean oil; and

> a pH modifier, wherein the pH modifier is sodium oleate;
> wherein the pH of the composition ranges from 7.5 to 9.0,
> wherein the ratio of egg yolk lecithin to aprepitant (wt %:wt %) ranges from about 18:1 to 22:1.

'794 patent, cl. 1 (emphasis added to designate disputed limitation).

Claim 1 of the '465 patent recites as follows:

> 1. A method for *preventing or treating* a subject at risk of or suffering from emesis, comprising administering to the subject a composition comprising an injectable *physically stable* emulsion wherein the emulsion comprises:
> aprepitant;
> 11 wt/wt % to 15 wt/wt % of an emulsifier; an oil;
> a co-emulsifier which is an alcohol; a tonicity modifier; a pH modifier; and water;
> wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1, and
> wherein the pH of the emulsion ranges from about 7.5 to 9.0.

'465 patent, cl. 1 (emphasis added to designate disputed limitations).

In their joint claim construction chart, the parties identified disputes regarding the construction of three terms that appear in the asserted claims. Dkt. No. 42. The parties subsequently filed briefs outlining their positions with respect to each of those terms. Dkt. Nos. 45, 47, 49, 51. On July 24, 2023, I held a claim construction hearing. I address below each of the disputes raised in the parties' briefs and at the hearing.

A. "physically stable"

The term "physically stable" appears in claims 1 and 8 of the '794 patent, claim 1 of the '465 patent, claims 1 and 15 of the '793 patent, claim 1 of the '208 patent, and claim 1 of the '018 patent, as well as the claims that depend from each of those independent claims. Heron proposes that the term be construed to mean: "Meets the criteria under USP<729>[1] for mean droplet size not exceeding 500 nm and PFAT5 not exceeding 0.05%, and no visible aprepitant crystals when

[1] "USP <729>" refers to Chapter 729 of the United States Pharmacopeia, titled "Globule Size Distribution in Lipid Injectable Emulsions." That chapter has been introduced into the record by Heron and can be found at Dkt. No. 45-1, Exh. 11.

viewed at magnification of 4x to 10x, upon storage at 5ºC or room temperature for a period equal to or at least one week." Dkt. No. 45 at 6. Fresenius argues that the term is indefinite, and that "the PFAT5 component" of Heron's proposal should not be included in the court's construction in any event. *Id.*

As the specification of the '229 patent explains,[2] "[l]iquid formulations of aprepitant are very challenging to make" because aprepitant molecules have "poor solubility and poor permeability characteristics." '229 patent, col. 1, ll. 50–52. The inventors of the asserted patents sought to address that challenge by developing an emulsion that would "allow preparation of an injectable formulation as well as enhance bioavailability of the aprepitant once administered." *Id.* at col. 1, ll. 52–56.

One problem with emulsions generally is that "[a]ll true emulsions are thermodynamically unstable and may over time undergo a range of processes which tend to increase the droplet size." *Id.* at col. 2, ll. 3–5. As noted in the '229 patent specification, however, to be useful emulsions must be physically stable so as to remain injectable for a reasonable period of time. *Id.* at col. 2, line 1. Thus, the inventors sought to disclose a formulation that "allow[s] aprepitant to be incorporated into an emulsion for intravenous injection and remain stable during the shelf life of the formulation." *Id.* at col. 2, ll. 32–34. The asserted claims incorporate this feature by requiring that the claimed compositions be "physically stable" as that term is defined in the specification. *See, e.g.*, '794 patent, cl. 1.

The term "physically stable" is defined in the common specification of the asserted patents as follows:

[2] All the asserted patents have substantially the same specification, so all references to the specification in this order are to the '229 patent specification.

> "Physically stable" emulsions will meet the criteria under USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 µm and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 µm (PFAT5) not exceeding 0.05%, at 5° C. or room temperature for a designated storage time period. In addition, physically stable emulsions will have no visible aprepitant crystals upon storage at 5° C. or room temperature for a designated time period. Crystals are considered visible when viewed at magnification of 4x to 10x. An emulsion is physically stable if it meets the criteria under USP <729> and aprepitant crystals are not visible upon storage at 5° C. or room temperature for a time period equal to or at least 1 week, 2 weeks, 4 weeks, 1 month, 2 months, 6 months, 1 year or 2 years.

'229 patent, col. 8, ll. 5–21.

Heron's proposed construction tracks the characteristics of emulsions that the '229 patent specification describes as "physically stable." *See* Dkt. No. 45 at 7. Specifically, Heron identifies three requirements as defining the term "physically stable" for purposes of the asserted patents: (1) the mean droplet size of the emulsion may not exceed 500 nm; (2) the PFAT5 percentage may not exceed 0.05 percent; and (3) no aprepitant crystals may be visible when the emulsion is viewed at a magnification of 4x to 10x. *Id.* Those three requirements must be measured "upon storage at 5ºC or room temperature for a period equal to or at least one week." *Id.*

USP <729> provides methods "for determination of the mean lipid droplet diameter and the distribution of large-diameter globule sizes [i.e., PFAT5] in lipid injectable emulsions." Dkt. No. 45-1, Exh. 11, at 360. As recited in the first requirement of Heron's proposed construction, USP <729> states that "[t]he intensity-weighted mean droplet diameter (MDD) for lipid injectable emulsions must be less than 500 nm or 0.5 µm." *Id.* at 361. As recited in Heron's second proposed requirement, USP <729> states that "[t]he volume-weighted, large-diameter fat globule limits of the dispersed phase, expressed as the percentage of fat residing in globules larger than 5 µm (PFAT5) for a given lipid injectable emulsion, must not exceed 0.05%." *Id.* at 363. Neither Heron's third requirement, nor the temperature and timing requirements set forth in the specification, are expressly provided in USP <729>. Instead, they are discussed in column 8 of

the specification of the '229 patent and are adhered to in the various examples disclosed in the specification. '229 patent, col. 8, ll. 5–21; *id.* at col. 20, line 36, through col. 21, line 34.

1. Indefiniteness

Fresenius contends that the requirement that the claimed compositions be "physically stable" renders the claims indefinite because the term introduces subjectivity into the claims by raising questions about how stable a particular compound must be. As the Supreme Court has explained, a patent claim is indefinite if the patent "fail[s] to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). Fresenius raises three principal contentions in support of its argument that the claims are indefinite, none of which is persuasive.

First, Fresenius argues that Heron's proposed requirement that there be no visible crystals when the emulsion is viewed under magnification "rests solely on the subjective observation of the individual looking at an emulsion under magnification." Dkt. No. 47 at 7. According to Fresenius, that determination is indefinite because a determination whether an emulsion lacks visible crystals "would necessarily vary between observers." *Id.*

That argument is contrary to well-settled case law. In *Sonix Technology Co., Ltd. v. Publications International, Ltd.*, 844 F.3d 1370 (Fed. Cir. 2017), the Federal Circuit rejected a similar argument, and the court's analysis in that case is directly applicable here. In *Sonix*, the defendants argued that the term "visually negligible" rendered the asserted claims indefinite because the assessment of whether something is "visually negligible" would "depend[] on the 'vagaries of any one person's opinion.'" *Id.* at 1376–77. The court disagreed, noting that the determination of visual negligibility "involves what can be seen by the normal human eye," which provided "an objective baseline through which to interpret the claims." *Id.* at 1378; *see also*

Liqwid, Inc. v. L'Oréal USA, Inc., 720 F. App'x 623, 630 (Fed. Cir. 2018) ("Indefiniteness does not necessarily follow from a claim's reliance on visual inspection with the human eye."); *Acuity Brands Lighting, Inc. v. Ultravision Techs.*, No. 19-2207, 2021 WL 3187439, at *5 (D. Del. July 28, 2021); *f'real Foods, LLC v. Hamilton Beach Brands, Inc.*, 388 F. Supp. 3d 362, 365 (D. Del. 2019); *Integra LifeSciences Corp. v. HyperBranch Med. Tech., Inc.*, No. 15-819, 2017 WL 3336274, at *17 (D. Del. July 27, 2017) ("[T]he term 'observable change' is not purely subjective. It does not rely on a person's whimsical taste or opinion to give the term meaning; instead, it relies on a user's visual observation."); *Ansell Healthcare Prods. LLC v. Reckitt Benckiser LLC*, No. 15-915, 2017 WL 1021844, at *2 n.2 (D. Del. Mar. 16, 2017) ("A claim is not indefinite just because a person has to make a visual judgment.").

This case is almost identical to *Sonix*. Although there may be some edge cases in which certain crystals can be seen by some skilled artisans and not others, the existence of visible crystals in an emulsion would be a question that could be objectively answered by a skilled artisan based on what could be seen under magnification by a person of ordinary skill in the art with ordinary powers of visual perception. And to the extent that experts may reach different conclusions in this case about whether a particular emulsion contains crystals visible to an artisan of ordinary skill, that question is capable of being resolved by a factfinder.

The cases in which claims have been held indefinite due to subjectivity generally relate to claim limitations that call for subjective, opinion-based judgments. *See, e.g.*, *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1348–56 (Fed. Cir. 2005) (holding that the term "aesthetically pleasing" rendered the claims indefinite); *Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1371–73 (Fed. Cir. 2014) (holding that the phrase "in an unobtrusive manner that does not distract a user" rendered the asserted claims indefinite because the phrase was "highly

subjective"). This case is not like those; the visual acuity of an ordinary observer provides an objective standard for determining whether crystals are visible or not in a particular emulsion, in contrast to highly subjective judgments such as whether a feature is aesthetically pleasing or sufficiently unobtrusive not to be distracting.

Second, Fresenius argues that the references to multiple storage conditions and timing requirements in Heron's proposed construction inject fatal uncertainty into the construction of the asserted claims. Dkt. No. 47 at 8. Fresenius focuses on the portion of the definition of "physically stable" stating that to be deemed physically stable, an emulsion must meet the designated criteria "upon storage at 5° C. or room temperature for a time period equal to or at least 1 week, 2 weeks, 4 weeks, 1 month, 2 months, 6 months, 1 year or 2 years." '229 patent, col. 8, ll. 17–20. The temperature requirement is indefinite, according to Fresenius, because the definition does not state whether the specified conditions need be met at both 5° C. and room temperature, or whether it is sufficient if those conditions are met at either temperature. In addition, Fresenius argues, the storage period requirement is indefinite because the definition does not specify whether the emulsion must remain stable for one week or for any of the other periods set forth in the definition.

The definition of "physically stable" in the specification is not a model of patent drafting. From the remainder of the specification, however, it is evident that the patentee intended by those requirements that to be "physically stable," an emulsion would have to be stable for at least one week regardless of whether it was stored at room temperature or in refrigerated conditions at 5° C.

The definitional language at column 8 of the specification was clearly based on the results of tests conducted on four emulsions, the results of which were reported in columns 15 through 21 of the specification. The compositions and methods of preparing those four emulsions were described in Examples 1, 2, 3, and 6 in the specification. *See* '229 patent, col. 16, line 1, through

col. 18, line 15; *id.* at col. 19, line 31, through col. 20, line 30. Example 7 reported the stability periods for each of those compositions. The reported stability periods ranged from 2 to 3 months when the emulsion was stored at 25° Celsius (approximately room temperature) to more than 10 months when the emulsion was stored at 5° Celsius (a typical refrigerator temperature). *See* '229 patent, col. 20, line 31, through col. 21, line 11. Those references to the storage temperatures indicate the length of the period of physical stability for each of the tested emulsions when stored in two common manners—either at room temperature or in typical refrigerated conditions. By contrast, the formulations disclosed in Examples 4 and 5, which Heron characterizes as representing prior art emulsions, lost physical stability quickly, with observable crystals developing within four days after preparation when stored at room temperature. *See* '229 patent, col. 18, line 16, through col. 20, line 26.

With regard to Fresenius's argument that it is unclear whether the claimed emulsion must remain stable at either 5° Celsius or at room temperature, or whether those conditions must be satisfied at both temperatures, the answer given by the specification is that the latter is intended. To begin with, the language of the specification strongly suggests that the emulsion must remain stable whether stored at 5° Celsius or at room temperature. Moreover, the specification reports that the emulsions of Examples 4 and 5 failed to satisfy the crystal size requirement within four days when stored at room temperature. *See* '229 patent, col. 18, ll. 44–46; col. 19, ll. 12–14. There was no report of testing those emulsions at 5° Celsius. The clear implication is that a failure to maintain physical stability for at least a week at room temperature was enough to disqualify the emulsions of Examples 4 and 5. For those reasons, it is clear that the references in column 8 to storage at either 5° Celsius or room temperature contemplated that the emulsion would have to remain physically stable for the designated period at each of those storage temperatures. That is,

the requirement that the population of large-diameter fat globules "not exceed[] 0.05% at 5° C. or room temperature," and that "physically stable emulsions will have no visible aprepitant crystals upon storage at 5° C. or room temperature" requires that those conditions be met at both storage temperatures. *See id.* at col. 8, ll. 9–15. Interpreting the specification to require both conditions to be satisfied is consistent with the general principle that the word "or" is ordinarily given a "conjunctive interpretation" when it follows a negative, as in this case. *See Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 680 (Fed. Cir. 2015). The temperature provisions of the "physically stable" definition are therefore not indefinite.

With regard to Fresenius's argument as to the timing requirements, the specification states that the determination of physical stability must be made after a time period "equal to or at least 1 week, 2 weeks, 4 weeks, 1 month, 2 months, 6 months, 1 year or 2 years." '229 patent, col. 8, ll. 19–21. Fresenius suggests that there may be uncertainty about the scope of the claim in a situation in which, for example, an emulsion was stable after one week but not after two weeks. Dkt. No. 47 at 8.

Fresenius's argument is unconvincing. The clear intent of the sentence in the specification that recites those time periods is to indicate that it is ideal if an emulsion is stable for up to two years, but that the emulsion is deemed "physically stable" for purposes of the asserted claims if it satisfies the appropriate requirements for at least one week. The specification does not evince any intent to limit the scope of the claims beyond the one-week standard. In the case posed by Fresenius, the emulsion would thus be deemed physically stable if it were stable after one week, but not after two.

In its sur-reply brief, Fresenius points out that in column 14 of the '229 patent, lines 53 through 57, the specification states that "[a] physically stable emulsion of the invention is one

which can be stored under appropriate conditions for at least 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, 24, or 36 months, without an increase in average droplet size above that allowed as stated in USP <729>." Fresenius notes that the reference to the minimum storage time in that passage (an emulsion "which can be stored under appropriate conditions for at least 1 . . . month[]") differs from the reference to the minimum storage time in the passage that defines "physically stable" at column 5, lines 5 through 21 (an emulsion that can be stored "at 5° C. or room temperature for a time period equal to or at least 1 week . . . ."). That inconsistency, Fresenius argues, contributes to the indefiniteness of the claims containing the "physically stable" limitation.

While the apparent inconsistency in the characterization of the term "physically stable" in columns 8 and 14 of the specification suggests clumsiness in drafting, it is reconcilable. The definition in column 8 requires that the emulsion be stable for a period of at least one week at two specific temperatures. The reference in column 14 states that a physically stable emulsion is one that can be stored for at least one month "under appropriate conditions." '229 patent, col. 14, ll. 54–55. The "appropriate conditions" could include temperatures lower than the 5° C. or room temperature posited in the definition of "physically stable" in column 5. Because the specification makes clear that the duration of the stable state of the emulsion increases with lower temperatures, *see id.* at col. 20, line 31, through col. 21, line 10, the requirement that the emulsion be physically stable for at least one month "under appropriate conditions" is not inconsistent with the requirement that it be stable for at least one week at the temperatures specified in column 8.[3] In

[3] While the two references to "physically stable" emulsions can be reconciled, the true explanation for the apparent inconsistency would appear to lie elsewhere. Notably, the definition of "chemically stable" at column 8, lines 22–30, of the '229 patent specification states in part that the emulsion remains stable "under appropriate storage conditions for at least 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, or 24 months." That is almost exactly the same language that is used in column 14 to describe physically stable emulsions. It may well be that the reference to physical stability in column 14 inadvertently conflated the requirements of physical stability and chemical stability. If

any event, the definitional provision at column 8 of the specification provides an explicit definition of "physically stable," and a person of ordinary skill in the art would understand that definition to be the governing definition for purposes of the asserted patents that contain a requirement of physical stability.

Third, Fresenius complains that USP <729> provides for different approaches to testing the criteria for physical stability. For that reason, Fresenius suggests that there is a "possibility for inconsistent results." *Id.* For example, USP <729> provides that mean droplet size can be measured using two different tests—dynamic light scattering or classical light scattering—and that globule size and distribution must be determined using a third test for measuring the amount of PFAT5 in the emulsion. Dkt. No. 45-1, Exh. 11, at 360–62. As the Federal Circuit has noted, however, "the mere possibility of different results from different measurement techniques" does not render a claim indefinite. *Takeda Pharm. Co. v. Zydus Pharms. USA, Inc.*, 743 F.3d 1359, 1366–67 (Fed. Cir. 2014); *see also Ethicon Endo-Surgery, Inc. v. Covidien, Inc.*, 796 F.3d 1312, 1321–22 (Fed. Cir. 2015) ("[A]lthough there are different methods of measuring the claimed average pressures, each of these methods is designed to provide similar measurements, whereas the different methods of measurement in *Honeywell* [*International, Inc. v. International Trade Commission*, 341 F.3d 1332 (Fed. Cir. 2003)] produced widely varying results."). In order for the use of different measurement techniques to create an indefiniteness issue, there must be a showing that "application of the different methods [would] result in materially different outcomes for the claim's scope such that a product or method may infringe the claim under one method but not

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so, the language at column 14 can be regarded as the product of a scrivener's error and therefore not the source of true ambiguity in the meaning of the claim language "physically stable." Whatever the explanation for the language in column 14, a person of ordinary skill in the art would understand the definition of "physically stable" to be provided by the express definitional language found in column 8 of the specification and thus not to give rise to invalidity for indefiniteness.

infringe when employing another method." *Ball Metal Beverage Container Corp. v. Crown Packaging Tech., Inc.*, 838 F. App'x 538, 542 (Fed. Cir. 2020); *see also Vifor Fresenius Med. Care Renal Pharma Ltd. v. Lupin Atlantis Holdings SA*, No. 18-390, 2019 WL 4222673, at *5 n.6 (D. Del. Sept. 5, 2019) ("Defendants have not shown that different testing methods would produce different results."); *CyDex Pharms., Inc. v. Alembic Global Holding SA*, No. 19-956, 2020 WL 6393918, at *4 (D. Del. Nov. 2, 2020) ("When there are multiple methods for measurement, a party asserting indefiniteness must show that those methods result in different outcomes; that is, that measurement under one method could yield infringement while another measurement would not."). Fresenius has made no such showing in this case.[4]

In sum, with respect to the "physically stable" limitation, Fresenius has not shown that a skilled artisan would be uncertain as to the scope of the asserted claims. The patent specifications explain in detail what characteristics an emulsion must have to be deemed "physically stable." '229 patent, col. 8, ll. 5–21. And two of those characteristics mirror the standards described in USP <729>, a text that is expressly invoked in the specifications of the asserted patents. Dkt. No. 45-1, Exh. 11. In view of those disclosures, a skilled artisan would readily recognize what is meant by the term "physically stable" as that term is used in the asserted claims. The claims are therefore not indefinite.

[4] Moreover, as Heron pointed out during the *Markman* hearing, to allege that the measurement methods identified in USP<729> for measuring mean droplet size are inconsistent would effectively be to question the USP<729> standard itself, which is a widely used industry standard for measuring the globule size distribution in an emulsion. Even if Heron had introduced some evidence suggesting inconsistency in the two measurement methods, that evidence would have to be sufficiently compelling to overcome the strong inference that both methods are sufficient to determine compliance with USP<729> given their express recitation in that standard.

2. The "PFAT5" Criterion

Fresenius next argues that the "PFAT5" portion of Heron's proposed construction should not be adopted because it is "inconsistent with the intrinsic evidence." Dkt. No. 47 at 10–11. In support of its argument, Fresenius first points out that during prosecution of the application that became the '465 patent, the applicants added the term "physically stable" to the claims to overcome a prior art rejection. Dkt. No. 47-1, Exh. A, at 2, 4–5. The applicants argued that the claimed emulsions were physically stable, while the emulsions disclosed in the prior art were not. Dkt. No. 47-1, Exh. G ¶ 9. The applicants' distinction over the prior art referred only to the fact that the prior art emulsion "form[ed] crystals within 4 days of storage at room temperature." The applicants did not discuss the mean droplet size or the PFAT5 percentage of the prior art emulsion. *Id.* Second, Fresenius contends that the examples in the specification of the '229 patent that relate to physical stability report only the mean droplet size of the tested emulsions and not the PFAT5 percentage of those emulsions. *See* '229 patent, col. 20, line 36, through col. 21, line 34.[5] Accordingly, Fresenius argues, it would be improper to interpret the term "physically stable," as that term is used in the claims, to mean that an emulsion must have a PFAT5 percentage that does not exceed 0.05%.

With respect to the first point, Fresenius points to a declaration from Thomas Ottoboni, one of the named inventors, that was submitted during prosecution of the application from which the '465 patent issued. In that declaration, Mr. Ottoboni argued that the claims in the application

[5] Fresenius overlooks that the discussion of Example 7 in the '229 patent states that the "percentage of fat globules above 5 µm," i.e., the PFAT5 percentage, was measured as part of that example. '229 patent, col. 20, ll. 40–43. Although the PFAT5 percentage for each sample was not reported in Table 7 of the '229 patent specification, *see id.* at col. 20, line 57, through col. 21, line 11, it is not the case, as Fresenius contends, that the examples in the '229 patent specification make no reference to the PFAT5 criterion for physical stability.

were distinguishable over a prior art reference, "Zhou," because emulsions prepared as taught by Zhou were "not stable" and "form[ed] crystals within 4 days of storage at room temperature." Dkt. No. 47-1, Exh. G ¶ 9. That is, Mr. Ottoboni contended that the emulsions of Zhou were not physically stable because they failed to satisfy the "no visible crystals" requirement for physical stability. Accordingly, there was no need for Mr. Ottoboni to discuss whether those emulsions satisfied the PFAT5 percentage requirement for physical stability. Mr. Ottoboni's failure to discuss the PFAT5 percentage of the emulsions of Zhou thus lends no support to Fresenius's position on this point.[6]

More generally, the problem for Fresenius is that the definition of "physically stable" set forth in column 8 of the '229 patent is a textbook example of lexicography. In the section titled "Definitions," the specification devotes an entire paragraph to explaining the criteria that must be satisfied for an emulsion to be deemed physically stable. '229 patent, col. 8, ll. 5–21. The inventors expressly chose to include the PFAT5 percentage as a criterion for determining whether an emulsion is "physically stable," and their choice will be respected in the court's claim construction. It is of no moment that some discussions of stability in the intrinsic records of the asserted patents do not make express reference to the PFAT5 criterion.

Accordingly, the court will adopt the essence of Heron's proposed construction of "physically stable" and will construe that term to mean: "Meets the criteria under USP<729> for mean droplet size not exceeding 500 nm and PFAT5 not exceeding 0.05%, and no visible

[6] In his declaration, Mr. Ottoboni also observed that the emulsions described in Examples 1, 2, 3, and 6 of the asserted patents' shared specification "were stable at room temperature for at least 2 months." Dkt. No. 47-1, Exh. G ¶ 9. That paragraph merely reflected the results disclosed in Table 7 of the specification in drawing a contrast between the Zhou reference and the applicants' emulsions; it did not amount to a disclaimer—as Fresenius suggested at the *Markman* hearing—of emulsions that were physically stable for time periods shorter than two months. *See* '229 patent, col. 20, line 57, through col. 21, line 11.

aprepitant crystals when viewed at magnification of 4x to 10x, after being stored either at 5º Celsius or at room temperature for a period of at least one week."

B. "treating" and "preventing"

Claim 1 of the '465 patent recites a method for "preventing or treating a subject at risk of or suffering from emesis," i.e., nausea and vomiting. That claim is the only independent claim in any of the asserted patents in which the term "preventing" appears. Claims 12 and 17 of the '229 patent, claims 12 and 17 of the '794 patent, and claim 1 of the '018 patent all recite "[a] method for treating nausea and vomiting in a subject in need thereof," but do not refer to "preventing" that condition.

Based on the meaning of the term "treatment" in the medical field, Heron argues that "treating" emesis, as used in the claims, means "caring for and managing a patient to combat, ameliorate, or prevent" nausea and vomiting. Dkt. No. 45 at 13 (citing *Treatment*, Mosby's Dictionary of Medicine, Nursing & Health Professions 1807 (2013), which defines "treatment" as "the care and management of a patient to combat, ameliorate, or prevent a disease, disorder, or injury").

As for "preventing," Heron argues that the term should be construed to mean "hindering the occurrence of or decreasing the incidence of." Again, Heron argues that its proposed construction accords with the plain and ordinary meaning of the term in the medical field. Dkt. No. 45 at 16 (citing *Preventive*, Mosby's Dictionary of Medicine, Nursing & Health Professions at 1452, which defines "preventive" as "pertaining to hindering the occurrence of an illness or decreasing the incidence of a disease").

In response, Fresenius contends that "treating" emesis does not include "preventing" that condition. According to Fresenius, "treating" emesis means "administering during or after the

occurrence of emesis or nausea and vomiting by the subject in order to lessen, control, mitigate, alleviate, or resolve the emesis, nausea, or vomiting." Dkt. No. 47 at 11. As for "preventing," Fresenius argues that the term means "administering before a potential risk of suffering from emesis to keep that event from happening." Dkt. No. 47 at 16.

Although Fresenius contends that the terms "treating" and "preventing" have "different meanings," Dkt. No. 47 at 13, Fresenius asserts that its construction "does not demand that the terms are mutually exclusive," *id.* at 14. It is unclear what Fresenius means by that disclaimer. By stating that the terms are not mutually exclusive, Fresenius appears to acknowledge that their meanings overlap to some degree, but Fresenius does not explain in what respects they overlap. In particular, Fresenius does not argue that the terms overlap by both including the prevention of emesis that has not yet manifested itself. In its sur-reply brief, Fresenius appears to reverse course and assert that the two terms are mutually exclusive. *See* Dkt. No. 51 at 7 ("[T]he term 'preventing' is different from, and not subsumed by, the term 'treating.'"). Fresenius did not offer much clarity on this point at the claim construction hearing, but the general thrust of its position appears to be that the two terms are mutually exclusive. Heron does not suggest that the terms "treating" and "preventing" mean the same thing; in Heron's view the term "treating" is broader than the term "preventing," and encompasses that term.

Non-technical, general-purpose dictionaries define the word "treat," in the context of medical treatment, to mean "to seek cure or relief of (as a disease)." *Treat*, Webster's Third New Int'l Dictionary 2435 (2002); *see also Treat*, Merriam-Webster's Collegiate Dictionary 1333 (11th Ed. 2020) ("to care for or deal with medically or surgically"); *Treat*, New Oxford American Dictionary 1844 (3d ed. 2020) ("to give medical attention to try to heal or cure"); *Treat*, Random House Webster's Unabridged Dictionary 2015 ("to deal with (a disease, patient, etc.) in order to

relieve or cure"). The word "prevent," by contrast, is generally understood to mean "to keep from happening or existing esp. by precautionary measures" or to "make impossible through advance provisions." *Prevent*, Webster's Third New Int'l Dictionary at 1798; *see also Prevent,* Merriam-Webster's Collegiate Dictionary at 984 ("to keep from happening, hinder, stop"); *Prevent*, New Oxford American Dictionary at 1384 ("to keep (something) from happening or arising"); *Prevent*, Random House Webster's Unabridged Dictionary at 1535 ("to keep from occurring; avert; hinder").

Medical dictionaries support Heron's contention that the term "treatment" is given a broad definition in the medical field, which can include prevention. Mosby's Dictionary of Medicine defines "treatment" to include the care of a patient to "prevent a disease, disorder, or injury." *Treatment*, Mosby's Medical Dictionary 1799 (10th ed. 2017). Other medical dictionaries contain similarly broad definitions of the term "treatment," to include "medical or surgical management of a patient," Stedman's Medical Dictionary 2022 (28th ed. 2006), and "the management and care of a patient for the purpose of combating disease or disorder," Dorland's Illustrated Medical Dictionary 1927 (33d ed. 2020). And both the Stedman and Dorland dictionaries include "preventive treatment" as a subcategory of treatment. The Stedman dictionary, for example, defines preventive treatment as "[t]he institution of measures designed to protect a person from an attack of a disease to which the person has been or is liable to be exposed." *See Preventive Treatment*, Stedman's Medical Dictionary at 2023. A fair summary of the definitions in the medical dictionaries is that the term "prevention," as used in the medical field, refers to keeping a disease or other medical condition from occurring or getting worse, while the term "treatment," as used in the medical field, is defined more broadly to include administering a drug or other form of

intervention in order to have some beneficial effect with respect to a disease or medical condition. Treatment, as used in the medical profession, thus can include preventive measures.

Examination of the common specification of the asserted patents makes it clear that the patents do not draw a crisp distinction between the prevention and treatment of emesis and do not treat the two as mutually exclusive. Column 1 of the '229 patent specification states that the disclosure in the patent "relates generally to emulsions and systems for the intravenous or parenteral administration of aprepitant *for treatment of emesis*." '229 patent, col. 1, ll. 15–17 (emphasis added). A few lines later, the specification states that aprepitant "is intended for *the prevention of acute and delayed nausea and vomiting* associated with initial and repeat courses of highly emetogenic cancer chemotherapy." *Id.*, col. 1, ll. 42–44 (emphasis added). In that context, it is evident that the specification refers to "treatment" as denoting measures having beneficial effects with respect to nausea and vomiting, and "prevention" as denoting means that hinder the onset of nausea and vomiting.

The specification uses the term "prevention" in only one other passage, where the specification alludes to the "medical use" of the disclosed formulations. *See* '229 patent, col. 15, ll. 42–62. In that passage, the specification states that the disclosed compositions "can be used for the prevention or treatment of emesis" in patients "undergoing highly or moderately emetogenic chemotherapy." *Id.*, col. 15, ll. 46–52. The specification further asserts that the disclosure "encompasses a method of treatment" and relates to the use of the disclosed formulations "for use preventing or treating emesis in a subject in need thereof." *Id.*, col. 15, ll. 55–56.

Fresenius argues that the reference to "prevention or treatment of emesis" in that passage and in claim 1 of the '465 patent ("A method of preventing or treating a subject at risk of or suffering from emesis") indicates that "treatment" and "treating" cannot wholly encompass

"prevention" and "preventing." Dkt. No. 47 at 12–13. But Heron does not argue that the terms are wholly congruent. Heron's argument is that the term "treatment" in this context is a broader term that includes the use of aprepitant to prevent emesis in a patient who is receiving chemotherapy.

There is particular force to Heron's argument in the context of the treatment to which the asserted patents are directed. The patents at issue in this case are addressed to the treatment and prevention of a side effect of chemotherapy, which is itself a treatment of a different condition. In this context, it is entirely reasonable to regard "treatment" to include a preventive measure directed to a common side effect that results from the broader treatment regimen administered to cancer patients. In claim 1 of the '465 patent, the words "[a] method for preventing or treating a subject at risk of or suffering from emesis" are therefore best understood as serving a "belt and suspenders" purpose, designed to ensure that the claim would be interpreted to cover the use of the method for chemotherapy recipients, either before or after the onset of nausea and vomiting.[7]

Beyond that, the prosecution history demonstrates that the term "treating" has been understood, in the context of caring for chemotherapy patients, to include measures taken in advance to prevent emesis. In particular, Heron notes that the examiner issued a double-patenting rejection over the claims of the '793 patent because "[t]he ordinary artisan in the medical arts recognizes that aprepitant is used for treating nausea and vomiting because it is the only FDA approved medication for the prevention of postoperative nausea and/or vomiting." Dkt. No. 45-1,

[7] Fresenius argues (Dkt. No. 47 at 13) that the word "or" in the phrase "method for preventing or treating" in claim 1 of the '465 patent designates alternatives. *See, e.g.*, *Wasica Fin. GmbH v. Cont'l Auto. Sys.*, 853 F.3d 1272, 1280 (Fed. Cir. 2017); *Kustom Signals, Inc. v. Applied Concepts, Inc.*, 264 F.3d 1326, 1331 (Fed. Cir. 2001). While the word "or" is often used to designate alternatives, it is not the case that in such a situation the two alternatives may not overlap in any respect. That is particularly true when applying such a rule would lead to a result that is inconsistent with the plain and ordinary meanings of the terms.

Exh. 23, at 5. Thus, the examiner's comments indicate that the examiner understood the phrase "treating nausea and vomiting" to include preventing the occurrence of nausea and vomiting that would otherwise result from the administration of a chemotherapy regimen.

Looking outside the evidence relating to the patents, Fresenius argues that the label for Heron's branded drug CINVANTI indicates that "treating" emesis does not encompass "preventing" the condition. The label explains that CINVANTI is used "for the prevention of" nausea and vomiting, but it also notes that CINVANTI "has not been studied for treatment of established nausea and vomiting." Dkt. No. 47-1, Exh. H, at 1. In view of those comments in the CINVANTI label, Fresenius argues that "treating" must be viewed as a distinct claim term that does not encompass "preventing."

Heron responds that the portion of the CINVANTI label cited by Fresenius does not bear directly on the meaning of those terms in the asserted patents. Heron explains that the label merely states that CINVANTI has not been studied for the treatment of "established" nausea and vomiting, i.e., the effectiveness of CINVANTI in combating emesis has not been tested on patients who have already developed nausea and vomiting. Moreover, Heron points out that CINVANTI has been studied for the prophylactic treatment of patients at risk of developing those symptoms, and the CINVANTI label, which is directed to the "prevention of CINV" repeatedly refers to "treatment with CINVANTI." Dkt. No. 49 at 13–14 (citing Dkt. No. 47-1, Exh. H, at 5–8, 10, 12, 19–25). The use of the term "treatment" in that context indicates that the label understands "treatment" to encompass "prevention." The reference to the absence of testing for "established nausea and vomiting" in the CINVANTI label therefore does not undermine Heron's contention that "treating" a patient at risk of suffering from emesis includes treatment that is designed to prevent emesis that has not already emerged. In any event, the qualification found in the CINVANTI label relates to

the testing done as part of the FDA approval process; it does not address the scope of the term "treating" as used in Heron's patent, and it provides no support for Fresenius's claim that "treating" emesis, as used in the '465 patent, should be interpreted to exclude "preventing" emesis.

For the foregoing reasons, the term "treating," as used in the asserted patents, will be interpreted to mean caring for and managing a patient to combat, ameliorate, or prevent emesis, and the term "preventing," as used in the asserted patents, will be construed to mean hindering the occurrence of emesis.

IT IS SO ORDERED.

SIGNED this 31st day of July, 2023.

William C. Bryson

WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE